Trophic ecology, behaviour and host population dynamics in Echinococcus multilocularis transmission

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Abstract: The life cycle of the cestode Echinococcus multilocularis primarily involves canids and small mammals (rodents, lagomorphs) as definitive and intermediate hosts, respectively. Several surveys have identified marked temporal and geographical variations at different scales in the parasite's prevalence in both types of hosts, suggesting variations in the biological and ecological factors that control transmission processes. The parasite transmission from intermediate to definitive hosts is determined by the predator-prey relationship, which theoretically depends on prey population dynamics and the complex dietary response of predators to varying densities of prey species and other food items. Parasite eggs are transmitted to intermediate hosts via carnivore faeces, whose distribution in the environment is driven by the defecating behaviour of final hosts. We reviewed field-based studies that address issues related to the trophic ecology and behaviour of definitive hosts, interactions between definitive and intermediate hosts, and E. multilocularis transmission both in wild and domestic animals in rural and urban environments. Two density-dependent mechanisms control the transmission dynamics in definitive hosts: one is based on the variations in the availability of intermediate hosts, and the other is based on the variations in the density of the definitive host and its faeces. Non-linearity and the direct and delayed responses of definitive host contamination in relation to intermediate host population variations were recorded. The dietary response of the red fox was shown to be complex when abundant alternative resources were available (anthropogenic food, multiple intermediate host prey species). Micro-local hotspots of parasite transmission to intermediate hosts in a landscape, as well as areas of higher risk for human contamination in village and urban settings, may be explained by the definitive hosts' activity patterns and defecation behaviour.

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Trophic ecology, behaviour and host population dynamics in *Echinococcus multilocularis* transmission

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ABSTRACT

The life cycle of the cestode *Echinococcus multilocularis* primarily involves canids and small mammals (rodents, lagomorphs) as definitive and intermediate hosts, respectively. Several surveys have identified marked temporal and geographical variations at different scales in the parasite's prevalence in both types of hosts, suggesting variations in the biological and ecological factors that control transmission processes. The parasite transmission from intermediate to definitive hosts is determined by the predator–prey relationship, which theoretically depends on prey population dynamics and the complex dietary response of predators to varying densities of prey species and other food items. Parasite eggs are transmitted to intermediate hosts *via* carnivore faeces, whose distribution in the environment is driven by the defecating behaviour of final hosts. We reviewed field-based studies that address issues related to the trophic ecology and behaviour of definitive hosts, interactions between definitive and intermediate hosts, and *E. multilocularis* transmission both in wild and domestic animals in rural and urban environments. Two density-dependent mechanisms control the transmission dynamics in definitive hosts: one is based on the variations in the availability of intermediate hosts, and the other is based on the variations in the density of the definitive host and its faeces. Non-linearity and the direct and delayed responses of definitive host contamination in relation to intermediate host population variations were recorded. The dietary response of the red fox was shown to be complex when abundant alternative resources were available (anthropogenic food, multiple intermediate host prey species). Micro-local hotspots of parasite transmission to intermediate hosts in a landscape, as well as areas of higher risk for human contamination in village and urban settings, may be explained by the definitive hosts' activity patterns and defecation behaviour.

1. Introduction

The life cycle of the cestode *Echinococcus multilocularis* primarily involves canids and a large number of small mammal species (rodents, lagomorphs) as definitive and intermediate hosts, respectively (Rausch, 1995). The predator-prey relationship determines the transmission of the parasite from intermediate to definitive hosts, whereas the release of canid faeces in the environment allows the parasite's eggs to be transmitted to intermediate hosts.

Many publications have been issued over decades that report the local prevalence of the parasite in definitive (several species of foxes such as *Vulpes vulpes*, *Vulpes ferrilata* or *Vulpes lagopus*, raccoon dogs, coyotes, golden jackal, wolves and dogs) and intermediate host populations. Some authors have associated the variation in prevalence to the variations in host life-history traits (mostly age structure of populations) and/or in environmental parameters, such as climate, landscape characteristics or geographical location (for recent reviews see Atkinson et al., 2013; Otero-Abad and Torgerson, 2013). For example, a number of surveys on regional or national scales have identified a high spatial heterogeneity in the prevalence of the parasite in red fox (*V. vulpes*) populations (Miterpakova et al., 2006; Combes et al., 2012; Guerra et al., 2014). In a recent screening in the north-eastern half of France covering an area of 240,000 km^2, Combes et al. (2012) showed prevalence variation from more than 60% to less than 10% within only some tens of kilometres. At this spatial scale, differences in climatic conditions are

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not likely to explain such gradients. Instead, it has been proposed that small scale variations in the distribution, abundance and population dynamics of intermediate hosts (*e.g.* Guerra et al., 2014) and interactions between host populations *via* predator-prey relationship could play a critical role in the transmission intensity of the parasite (Giraudoux et al., 2003). On a more local scale, the transmission of the parasite's eggs to intermediate hosts is governed by the distribution of the definitive host's faeces in the environment and the micro-climatic conditions controlling egg survival (Giraudoux et al., 2002). The definitive hosts' defecating behaviour, and thus the patterns of environmental contamination, is determined by several factors, including habitat use, social interactions among congenerics, local habitat features and the distribution of resources in the environment. Here, we aim to review field-based studies that (1) correlate *E. multilocularis* prevalence in definitive hosts (foxes and dogs) in urban and rural environments to at least one of the following factors: small mammal intermediate host population density, definitive host population density or diet; (2) report definitive host faeces distribution or activity patterns in relation to environmental characteristics or to intermediate host spatial distribution (see Table 1 for a list of publications). We then highlight gaps in knowledge and propose research perspectives.

2. Intermediate host populations, predation and *E. multilocularis* prevalence in definitive hosts

2.1 E. multilocularis *transmission in foxes*

An early major contribution to the transmission ecology of *E. multilocularis* between small mammals and foxes was given by Saitoh and Takahashi (1998). They investigated *E. multilocularis* winter prevalence dynamics in a sample of 9828 foxes (*V. vulpes*) and *Myodes rufocanus* population variations in three localities of Hokkaido, the northernmost island of Japan, over 8 years. In this area, *M. rufocanus* populations were monitored by private foresters as part of the forest pest management programmes. The parasite prevalence in foxes greatly varied among years (average ranging between 20.2% and 44.7%) and was correlated with the *M. rufocanus* density of the current year in the three sites. Moreover, a delayed effect of vole abundance was suspected in Kushiro and Nemuro, where the parasite prevalence was also correlated with the intermediate host population density of the previous year. The effect of the current year vole density on prevalence was attributed to the direct dietary response of the fox to its main prey density variation: if the fox consumption rate on the prey is dependent on its density, the parasite transmission intensity to foxes should be as well. The one year-delayed effect observed in the two sites was attributed to the effect of the lower snow cover in winter that allowed foxes to hunt more easily on rodents, compared to the third site where a thick snow cover prevented predation and drastically reduced transmission. Thus, differences in the winter food habits of foxes may explain differences in the overwintering patterns of the parasite. In this study, the hypothesis on transmission mechanisms was grounded on fox dietary studies undertaken in the 1970s and 80s, but no data on the fox diet collected in parallel to prevalence and intermediate host density were available to confirm or reject those hypotheses. In the northern ecosystem of Spitsbergen, Svalbard, Stien et al. (2010) reported an average 8.5% *E. multilocularis* prevalence in 353 Arctic foxes (*V. lagopus*, formerly known as *Alopex lagopus*). They showed that prevalence significantly decreased with increasing distance from the *Microtus levis* population (formerly known as *M. rossiaemeridionalis*), known to be the only intermediate host (with a 19% average parasite prevalence).

The landscape composition of the mid-altitude plateau of the Jura Mountains in eastern France is dominated by grassland and is favourable to regular and spatially asynchronous population outbreaks of two grassland rodent species, *Arvicola scherman* (formerly *A. terrestris*) and *Microtus arvalis* (Delattre et al., 1999; Giraudoux et al., 1997; Raoul, Defaut et al., 2001), which are considered the main *E. multilocularis* intermediate hosts in Europe and an important food resource for foxes. This place is located in the historical area of higher endemicity of Western Europe, and the average parasite prevalence in fox populations ranged from 20% to 65% (Raoul, Deplazes et al., 2001). Based on the copro-ELISA diagnostic on 1252 faeces collected in the field, Raoul et al. (2010) showed that *E. multilocularis* infection in foxes was asymptotically related to both *A. scherman* and *M. arvalis* relative density in the field, suggesting a non-linear parasitic response: infection rose quickly up to a plateau that may be partly attributed to immunity mechanisms regulating infection level. In the Slovak Republic, 3096 red foxes were collected in the entire country between 2000 and 2004 and analysed for *E. multilocularis* infection using the sedimentation and counting technique (Miterpakova et al., 2006). In a sub-sample of foxes from southern and northern regions the prevalence of *E. multilocularis* was correlated with the density of small mammals, although the species actually trapped were not identified by the authors.

The transmission of *E. multilocularis* within large and medium cities, firstly reported in early 2000, represents a new context that should result from the general increase in fox populations worldwide. The urban cycle of the parasite is now documented in Zurich and Geneva (Switzerland), Stuttgart (Germany), Copenhagen (Denmark), Sapporo (Japan), Nancy, Annemasse and Pontarlier (France), and Calgary (Canada) (Hofer et al., 2000; Tsukada et al., 2000; Deplazes et al., 2004; Fischer et al., 2005; Robardet et al., 2008; Catalano et al., 2012; Comte et al., 2013). A general pattern that seems to emerge is a decrease in *E. multilocularis* prevalence in foxes according to the following gradient: rural periphery/residential peri-urban area/urban centre. The distribution of intermediate host populations has been investigated in Zurich and Nancy (Hegglin et al., 2007; Robardet et al., 2008) with similar findings (see Table 2 for a comparison between Zurich and Nancy cities, where key ecological parameters of the cycles have been documented). Indeed, one of the main fox prey species displayed a higher density in the rural periphery (*M. arvalis* in Nancy) and/or in the residential peri-urban area (*A. scherman* in Zurich) compared to the urban centre where the relative densities of both prey species were lower due to reduced availability of suitable habitats (grasslands) and the lower numbers of animals within these habitats. The spatial and temporal patterns of the cycle involving coyote (*Canis latrans*) as definitive host have been investigated in urban parks of the city of Calgary (Liccioli et al., 2014). There, *E. multilocularis* faecal prevalence peaked in spring (43.47% of positive faeces) and strongly varied across parks, ranging between 5.34% and 61.48%. Higher faecal prevalence in two parks was associated with both the local small mammal assemblage being dominated by species known to be intermediate hosts (*vs.* non intermediate hosts) and higher prevalence of the parasite in these intermediate hosts.

At least two non-exclusive ecological mechanisms are likely to explain the dependence of *E. multilocularis* prevalence in foxes to the intermediate hosts' density variations: the functional and numerical response of the predator. The numerical response is the capacity of a predator to change its population density through demographic (alteration of reproduction success) and aggregation (modification of spatial behaviour and aggregation to prey patches) processes according to the changes in its prey density (Ricklefs and Miller, 2000). The functional response reflects the variation of the predator's diet following the variation of the density of its prey (Arditi and Ginzburg, 2012). In the context of *E. multilocularis* transmission, a numerical response would theoretically lead to higher fox populations when prey density increases, thereby increasing

Table 1
Summary of field-based studies addressing *Echinococcus multilocularis* prevalence in definitive hosts according to small mammal intermediate host population density, definitive host population density or diet, or definitive host faeces distribution/activity pattern in relation to environmental characteristics or intermediate hosts spatial distribution.

Country, region	Ecosystem	DH (diagnostic method)	IH density	DH predation on IH	DH density	DH faeces distribution	DH activity patterns	Reference
Spitsbergen, Svalbard	High arctic island	*V. lagopus* (SCT)	*Microtus levis* (location of the main vole colony)	No	No	No	No	Stien et al. (2010)
Alaska, St. Lawrence Island	Tundra	*V. lagopus* (necropsy)	*Microtus oeconomus* (trapping)	Yes (stomach content)	No	No	No	Rausch (1995) (synthesis)
Japan, Hokkaido	Rural	*V. vulpes* (necropsy)	*Myodes rufocanus* (trapping)	No	No	No	No	Saitoh & Takahashi (1998)
Switzerland, Grisons canton	Alpine landscape	*V. vulpes* (SCT)	No	Yes (stomach content)	No	No	No	Tanner et al. (2006)
Slovak Republic	Whole country	*V. vulpes* (SCT)	Species list not reported (trapping)	No	No	No	No	Miterpakova et al. (2006)
Switzerland, Zurich	Urban and peri-urban	*V. vulpes* (SCT)	*Microtus arvalis*, *Arvicola scherman* (transects)	Yes (stomach content)	No	No	Yes (radio tracking)	Hegglin et al. (2007)
Switzerland, Zurich	Urban and peri-urban	*V. vulpes* (copro-ELISA)	No	No	No	Yes (observations)	No	Stieger et al. (2002)
France, Lorraine	Urban and peri-urban	*V. vulpes* (copro-ELISA)	*Microtus arvalis*, *Arvicola scherman* (transects)	No	No	Yes (transects)	No	Robardet et al. (2011)
France, Lorraine	Urban and peri-urban	*V. vulpes* (SCT)	No	Yes (stomach content)	No	No	No	Robardet et al. (2008)
Japan, Hokkaido	Urban and peri-urban	*V. vulpes* (copro-ELISA)	No	No	No	Yes (around fox dens)	Yes (footprint survey)	Tsukada et al. (2000)
Japan, Hokkaido	Urban fringe (park)	*V. vulpes* (copro-ELISA and copro-PCR)	No	No	No	Yes (transects)	No	Lapaga et al. (2009)
Canada, Alberta	Urban parks	*C. latrans* (copro-PCR)	Small mammal community (trapping)	No	No	No	No	Liccioli et al. (2014)
Germany, Bavaria	Small towns and their periphery	*V. vulpes* (IST and copro-PCR)	No	No	No	No	Yes (radio tracking)	Janko et al. (2011)
France, Ardennes	Agricultural	*V. vulpes* (SCT)	*Microtus arvalis*, *Arvicola scherman* (transects)	Yes (stomach content and faeces analysis)	No	No	No	Guislain et al. (2008)

France, Ardennes	Agricultural	*V. vulpes* (SCT), see Guislain et al. (2008)	*Microtus arvalis*, *Arvicola scherman* (transects)	No	Yes (spotlight count)	Yes (transects)	No	Guislain et al. (2007)
France, Franche-Comté	Grasslands	*V. vulpes* (copro-ELISA)	*Microtus arvalis*, *Arvicola scherman* (transects)	No	Yes (spotlight count)	No	No	Raoul et al. (2003)
France, Franche-Comté	Grasslands	*V. vulpes* (copro-ELISA)	*Microtus arvalis*, *Arvicola scherman* (transects)	Yes (faeces analysis)	No	No	No	Raoul et al. (2010)
France, Franche-Comté	Grasslands	*V. vulpes* (no diagnostic)	Small mammal community (trapping)	No	No	Yes (transects)	No	Giraudoux et al. (2002)
China, Sichuan	High altitude plateau	*C. familiaris* (copro-PCR)	*Ochotona* spp., *Microtus* spp., *Cricetulus kamensis* (transects)	No	No	Yes (transects and quadrats)	Yes (GPS collar)	Vaniscotte et al. (2011)
China, Sichuan	High altitude plateau	*C. familiaris* (arecoline purge, copro-PCR)	No	Yes (questionnaire)	No	No	No	Budke et al. (2005)
China, Sichuan	High altitude plateau	*C. familiaris* (arecoline purge, copro-PCR)	*Ochotona* spp., *Microtus* spp. (transects)	No	No	No	No	Wang et al. (2007)
China, Sichuan	High altitude plateau	*C. familiaris* (arecoline purge, copro-PCR)	*Ochotona* spp., *Microtus* spp. (transects)	Yes (faeces analysis)	Yes (transect)	No	No	Wang et al. (2010)
Kyrgyzstan, Alay	High altitude plateau	*C. familiaris* (arecoline purge, copro-PCR)	No	Yes (questionnaire)	No	Yes (quadrats)	Yes (GPS collar)	Van Kesteren et al. (2013)
Kyrgyzstan, Naryn	High altitude plateau	*C. familiaris* (arecoline purge, copro-PCR)	No	Yes (questionnaire)	No	No	No	Ziadinov et al. (2008)

DH: definitive host, IH: intermediate host, SCT: sedimentation and counting technique, IST: intestinal scrapping technique.

Table 2
Comparison *of Echinococcus multilocularis* cycle characteristics between Nancy and Zurich.

			Zones		
			Rural	Peri-urban	Urban
E. multilocularis prevalence in red foxes		Z	63%	39%	16%
		N	54%	31%	4%
Prey density	*Microtus arvalis*	Z	●	●	●
		N	○ ○	○	○
	Arvicola scherman	Z	●●	●●●	●
		N	○	○	○
Fox diet	Arvicolids[a]	Z	●●●	●●●	●
		N	○ ○ ○	○ ○ ○	○
	Anthropogenic food	Z	●	●●	●●●
		N	○	○ ○ ○	○ ○ ○

Source: (from Hegglin et al., 2007; Robardet et al., 2008, 2011).
Z: Zurich, N: Nancy. Prey density comparisons are relevant only within the same site.
[a] *Arvicola scherman* and/or *Microtus arvalis* and/or *Myodes glareolus*.

the worm biomass within an area, giving rise to increased transmission intensity. In general, the numerical response of a predator is mediated by the availability of alternative prey and the ability of the predator to switch to them when the density of the main prey declines, which is the case for generalist predators. If it is not the case, the energy input to predators is not enough to maintain the population. The populations of *V. lagopus* in arctic ecosystems usually display a numerical response due to the low availability of alternative prey and the high amplitude of its main small mammal prey (*e.g.* the collared lemming *Dicrostonyx groenlandicus*) (Gilg et al., 2006). By contrast, there are apparently conflicting results about the ability of *V. vulpes* to display a numerical response: its density was not related to *A. scherman* density variations in the grassland plateau of the *E. multilocularis* endemic area of western Switzerland (Weber et al., 2002), whereas it displayed a numerical response in the Mediterranean scrubland of Spain after the collapse of its main prey, the European rabbit *Oryctolagus cuniculus* (Ferreras et al., 2011). One cannot formally exclude this mechanism to operate in *E. multilocularis* transmission, but field evidence was never provided on the variation in transmission as the consequence of the numerical response of the definitive hosts. The fox is by far the vertebrate predator whose diet has been best studied in a large panel of ecosystems, in many biogeographical areas and in every season; however, the fox functional response to prey variations is poorly documented. This also holds true for most predators and herbivores, which obscures our capacity to understand the ecology of trophically transmitted parasites. Only a few studies have investigated the relationship between *E. multilocularis* prevalence in definitive hosts and their predation patterns. A pioneer investigation of the ecology of the *E. multilocularis* natural cycle in the tundra ecosystem was undertaken by Robert Rausch in the 50s (for a synthesis see Rausch (1995)). On St. Lawrence Island, Alaska, the prevalence of the parasite in *V. lagopus* populations varied seasonally. The prevalence in 1579 foxes reached almost 100% in autumn, following several months during which their diet consisted mainly of the northern vole *Microtus oeconomus*. Additionally, almost all young foxes were infected by the time they left the den in late summer because they had been mostly fed on rodents and birds. Snow accumulation during winter reduced the accessibility to voles, and foxes had to switch to other resources such as carcasses of marine mammals. This resulted in reducing the prevalence to approximately 30% by the next spring. Such seasonal aspects are an important determinant of the transmission pattern of *E. multilocularis*. Low temperatures and humid conditions during the winter season can increase the survival of parasite eggs in the environment and lead to an accumulation of infective eggs during this period (Veit et al., 1995). Therefore it is not surprising that highest prevalence rates in intermediate hosts have been found in old overwintered individuals of *M. arvalis* in France (Delattre et al., 1988) and *A. scherman* in Switzerland (Burlet et al., 2011).

In the Swiss canton of Grisons in the Alps, which is located at the southern limit of the parasite distribution in Europe, Tanner et al. (2006) analysed both the prevalence of *E. multilocularis* on a 10×10 km grid pixel in 543 necropsied foxes and the presence of small mammals in fox stomach contents. The average frequency of prey occurrence in fox stomachs was highest for *Microtus*/*Pitymys* genera (19.6%), followed by *Myodes glareolus* (8.0%) and *A. scherman* (0.4%). The only significant statistical correlation (positive) was obtained between *E. multilocularis* prevalence in foxes and the predation of *Microtus*/*Pitymys* genera. The predation on other taxa (*M. glareolus*, *Arvicolidae*, *Muridae* and *Soricidae*) was not associated with variations in the parasite prevalence. In the mid-altitude plateau of the Jura Mountains in eastern France where *E. multilocularis* infection in foxes was asymptotically linked to *A. scherman* and *M. arvalis* density (see above), fox predation displayed a rather complex pattern (Raoul et al., 2010). The shape of the functional response to *A. scherman* density was sigmoid-like, typical of generalist behaviour; however, the predation rate on this species decreased when the density of *M. arvalis* – the other grassland species – increased, suggesting complex interactions among prey on the prey choice by the predator (Fig. 1a). No evidence of a functional response to *M. arvalis* density was provided: this species was consumed at a high level even when its density was very low (Fig. 1b). In the Ardennes, an endemic region of northeastern France where the prevalence of *E. multilocularis* in foxes is 53% (Guislain et al., 2008), the composition of the small mammal community differed from the Jura Mountains because the *A. scherman* populations are constantly at low density. A positive correlation between *M. arvalis* density and its frequency in fox diet was observed, whereas no correlation was detected for *A. scherman*, which was minimally consumed (Fig. 1c) (Guislain et al., 2008). A major difference between the two situations was the long-term population dynamics of the two rodent species, which were unstable, cyclic and prone to outbreaks in the Jura Mountains; they were much lower and stable in the Ardennes. This likely explained the differences in fox predation behaviour.

The fox diet in an urban transmission context has been investigated in Zurich and Nancy (Hegglin et al., 2007; Robardet et al., 2008). The presence of arvicolid rodents (*i.e. A. scherman* and *M. arvalis*, which were not distinguished) showed a strong contrast between the rural periphery and the residential peri-urban area, where their frequency in the diet was high (5–40% in Nancy and 70% in Zurich), and the urban centre, where the score was much lower (less than 5% in Nancy and 30% in Zurich). An inverse gradient was observed for the consumption of food from anthropogenic origin (*e.g.* food wastes, pet food). A synthetic view of transmis-

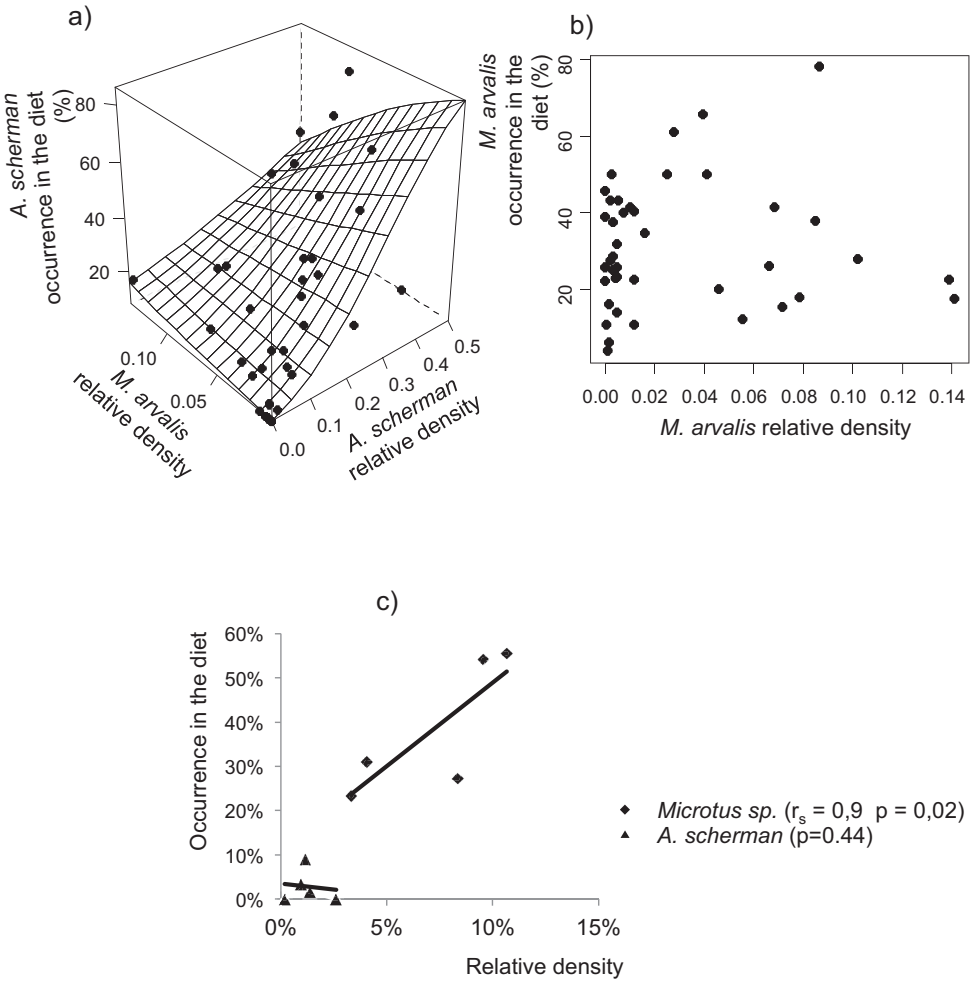

Fig. 1. Functional response of the red fox to *Arvicola scherman* and *Microtus arvalis* density variations in the Jura Mountains of eastern France (a and b) and in the Ardennes region of northeastern France (c). Grid in (a) represents the prediction from the statistical model.
Souce: (from Guislain et al., 2008; Raoul et al., 2010; reprinted with permission).

sion patterns characteristics in urban/peri-urban context is given in Table 2. Therefore, the behavioural plasticity of the fox allowed it to switch from a small mammal-based diet in the rural and peri-urban areas to anthropogenic food, which was shown to be more accessible and abundant in urban centres (Contesse et al., 2004). This functional response probably negatively affected the parasite dynamics in the city centre and could explain the very sharp decline in the infection rate in foxes within a very short distance of only 500 metres (peri-urban zone >60%, urban zone <20%; Hegglin et al., 2007). This distance roughly corresponds to the mean diameter of a fox home range in the city of Zurich (mean MCP for resident females and males: 29 and 31 ha) (Gloor, 2002).

2.2 E. multilocularis *transmission in dogs*

The effect of intermediate host density on a dog's diet and *E. multilocularis* transmission have received far less attention, although contact with dogs is identified as a major risk factor for human alveolar echinococcosis (Kern et al., 2004). A few studies investigated the contamination of dog populations with *E. multilocularis* on the mid- and high-altitude grasslands (2000–4500 m) of central Asia, including southeast Kyrgyzstan and central and western China (Sichuan, Qinghai and Xinjiang provinces) where pastoralism is the main activity (Budke et al., 2005; Wang et al., 2007, 2010; Ziadinov et al., 2008; Vaniscotte et al., 2011; Van Kesteren et al., 2013). These open landscapes are known to favour population outbreaks of a variety of small mammal species shown to be *E. multilocularis* intermediate hosts: *Ochotona curzoniae* and *Ochotona cansus*, *Microtus limnophilus*, *Cricetulus kamensis* in the eastern Tibetan plateau of central China, *Ellobius tancrei* and *Microtus gregalis* in Kyrgyzstan (Giraudoux et al., 2013). On the Tibetan plateau, Wang et al. (2007) showed that *E. multilocularis* prevalence in domestic dogs was positively associated with the relative density of small mammals living in common grasslands, a habitat where *Ochotona* sp. and *C. kamensis* population regularly reach high levels (Raoul et al., 2006; Giraudoux et al., 2013). Moreover, the *E. multilocularis* worm burden in dogs (mean = 39.64 worms) was positively correlated with the relative abundance of *Ochotona* sp. (Wang et al., 2010). Unfortunately, only the study by Wang et al. (2010) reported the diet of dogs in such ecological contexts: the presence of small mammal remains (bones and hairs) was identified in 28 out of 97 dog faeces samples collected in three villages of western Sichuan, but the low quality of bones did not allow precise identification of the prey species (*Ochotona* sp. teeth were retrieved from one sample). In the high plateau of Kyrgyzstan, Ziadinov et al. (2008) showed that domestic dogs that were allowed to completely roam or roam for part of the time and that were used for hunting were more likely to be infected with *E. multilocularis* based on arecoline purgation combined with PCR diagnosis (11% *vs.* 26% for tied and non-tied dogs, respectively). A similar result was observed on the eastern Tibetan plateau of western Sichuan (Budke et al., 2005). The hypothesis is that such dogs may have access to live or dead

small mammals during their activity. An investigation in Slovakia identified catching rodents as one of the main risk factors for dogs to be contaminated with *E. multilocularis*, but no information about the dog diet or small mammal population dynamics was available (Antolova et al., 2009).

3. Definitive host population density and *E. multilocularis* transmission

A decrease in the density of definitive hosts is likely to reduce the contamination of the environment with the parasite's eggs and thus the infection pressure to intermediate hosts. This would ultimately reduce *E. multilocularis* prevalence in intermediate hosts and the strength of the parasite cycle at the population level. In the high endemic area of the Jura Mountains, Raoul et al. (2003) monitored both the fox population level (using night roadside counts) and the contamination of foxes (using copro-ELISA on faeces collected in the field) in a 50 km^2 study site before, during and after the fox population crash due to secondary poisoning by bromadiolone, an anticoagulant used to control *A. scherman* population outbreaks. A sharp decline in the fox population occurred in 1997, when 30% of the grassland area was treated using bromadiolone and was followed with a one-year lag by the decrease in the contamination to a level comparable to that recorded in the low endemicity area (Raoul, Deplazes et al., 2001). This decline in the infection level of foxes in 1998 was concomitant with the high population peak of *A. scherman*, an intermediate host that has been shown to drive *E. multilocularis* infection in the area (see above). The *E. multilocularis* prevalence in fox populations in the study area of the Ardennes was 53% (Guislain et al., 2008), a score similar to the one observed in the traditional endemic area of the Jura Mountains (Raoul, Deplazes et al., 2001; Combes et al., 2012). However, the grassland rodent dynamics in the Ardennes was much more stable and lower on average (Guislain et al., 2008); there were no population outbreaks as observed in the Jura Mountains. The strong parasite transmission in the Ardennes is therefore probably not enhanced by intermediate host population dynamics. Instead, it can be hypothesised that the high infection level was the result of a sustainable high fox population density. Indeed, the fox density estimated using distance-sampling method varied between 3 and 4 individuals/km^2 (Guislain et al., 2007), which were the highest values recorded with the same protocol among 12 sites in northeast France (Ruette et al., 2003). Additionally, Reperant et al. (2009) showed in the city of Geneva, that in the part where sarcoptic mange was present (and accordingly lower fox density) the *E. multilocularis* prevalence in *A. scherman* was significantly lower. This suggests that more intensive transmission dynamics of the parasite can be due, temporally and/or spatially, either to a larger population of intermediate hosts or to a larger population of the definitive host population (or both).

On a larger spatial scale, a positive correlation between *E. multilocularis* prevalence in foxes and the fox annual hunting index in 13 cantons of Switzerland was reported by Ewald (1993). A similar pattern was obtained in southern Germany (Baden-Württemberg), where a concomitant increase in fox population density estimated using the hunting index and *E. multilocularis* prevalence in foxes was recorded (Romig, 2002). Those data should, however, be taken cautiously because intermediate hosts' population dynamics are likely to vary between cantons and regions and might act as a confounding factor. Moreover, hunting indexes suffer from several biases, such as spatial variability in hunting pressure, and cannot be accurately compared between areas.

The only data available for dogs is given by Wang et al. (2010) for the eastern Tibetan plateau of central China: *E. multilocularis* prevalence in dogs (mean = 14.8%) was positively associated with the number of dogs roaming freely within 200 m around the house of the dog keeper. This anecdotal information must however be considered cautiously because dogs may concentrate in patches of high densities of small mammals, which might be the dominant factor in controlling infection in dogs. However, even in areas where prevalence rates in dogs are generally very low (<1%), they have the potential to substantially contribute to the production of *E. multilocularis* eggs just because their density can be much higher than densities of local fox populations. Accordingly, Hegglin and Deplazes (2013) have calculated that in urban settings dogs can excrete up to 19% of the local *E. multilocularis* egg biomass even if the estimated prevalence is only 0.3%. Nevertheless, the contribution to the parasite transmission depends also to a large extent where the dogs defecate and to what extent dog owners remove the faeces of their dogs.

4. Definitive host activity patterns, defecation behaviour and *E. multilocularis* environmental contamination

4.1. Countryside environments

In the endemic area of Ardennes (France), Guislain et al. (2007) modelled the distribution of fox faeces on a local scale against several explanatory variables: site, month, precipitation, temperature, micro-scale habitat type and relative density of *A. scherman* and *M. arvalis*. The best-fit model retained the site, month, precipitation and micro-scale habitat variables. Thus, faeces density was higher in spring than in autumn and decreased according to the following habitat gradient: edges, road banks, hedges, inside habitat patches. There, medium-height vegetation edges and road banks were habitats where the density of *A. scherman* and *M. arvalis* was higher. If we assume that the proportion of infected faeces is not habitat-dependent and the microclimatic conditions are favourable to egg survival, then the risk of parasite transmission to intermediate hosts should be higher in these two micro-scale habitats (Guislain et al., 2007). In the Jura Mountains, *E. multilocularis* prevalence in rodents was very low on a regional scale (approximately 1‰) (Giraudoux et al., 2002). There, foxes have their dens mainly in forests, but more than 90% of their faeces were deposited in open habitats (grassland landscape) while foraging at night, and faeces density was highest along ploughed field borders and road verges compared to other habitats (16, 14 and 3 faeces per 10 km of transect, respectively (Giraudoux et al., 2002)). Small mammal trapping revealed that ploughed field borders were microhabitats where the percentage of trap lines having caught one or more infected animal was highest (7.3%) and where *E. multilocularis* prevalence was 12.6% (Giraudoux et al., 2002). It was suggested that these microhabitats were highly conducive for small mammal contamination due to both high fox faeces density and the possibility of egg burial *via* regular ploughing that preserved parasite eggs from desiccation.

4.2. Small villages and surrounding environments

The distribution of carnivore faeces and the activity patterns of dogs in the villages of the high altitude endemic areas of the eastern Tibetan plateau in China and of southeast Kyrgyzstan were quantified by Vaniscotte et al. (2011) and Van Kesteren et al. (2013), respectively. The density of faeces measured using quadrat counts was highly variable (median ranged between 22 and 120 faeces/ha), differed among villages and was generally higher in May than October in Kyrgyzstan (Van Kesteren et al., 2013). By contrast, no difference in faeces density was observed between villages and sampling years in China. The density of dog faeces significantly decreased with increasing distance from households, with a maximum at 50 m from houses (one quadrat reached a score of 354 faeces/ha) and a minimum of less than 14 faeces/ha in quadrats

located farther than 200 m (Vaniscotte et al., 2011). The proportion of copro-PCR positive faeces did not vary between samples collected within and outside villages in China (37/180). In these situations, the density of dog faeces can be very high, and the large majority of dog faeces were released in the vicinity of households, which probably constitutes an area at high risk for human contamination. The median distance travelled per dog from the household in Kyrgyzstan significantly varied among villages (range: 20–62 m), with maximum distances as high as almost 2 km (Van Kesteren et al., 2013). In China, 50% of GPS-collared dogs spent 80% of their time (core area) within less than 0.16 ha and did not travel more than 36 m away from the owner's house (Vaniscotte et al., 2011). However, a few dogs per village had an excursive behaviour and travelled more than 500 m away from their release point. Interestingly, the relative density of small mammals in the excursive areas (15.5–56.6% of positive transect intervals) was significantly higher than in the core areas (2.9–36.8% of positive transect intervals) (Vaniscotte et al., 2011). It is therefore suspected that domestic dogs spent part of their time in areas outside villages where they could predate small mammals.

4.3. Urban and peri-urban environments

Sapporo is a large city with a population of approximately 1.8 million located in the island of Hokkaido (Japan). Tsukada et al. (2000) analysed the distribution of foxes by detecting fox footprints in winter in 130 parks and woodlands evenly distributed within the city and sampled fox faeces in approximately 19 fox dens in the area. Significantly more footprint-positive parks and woodlands were located in the peripheral area (47.6%) than in the urban centre (22.9%), and copro-ELISA positive faeces were collected in 11 out of 19 dens, with only one located in the urban centre. There, the main *E. multilocularis* worm biomass was therefore probably present in the peripheral area, which is in accordance with the contamination gradient reported in most cities. The Nopporo Forest Park (20.5 km^2) is located in the urban fringe of Sapporo city, 15 km away from the centre. Lagapa et al. (2009) quantified the distribution of fox faeces in several habitats. The average percentage of copro-ELISA positive faeces was 49%, and faeces samples were mostly collected in forest (almost 60% of the total number of faeces found) and open-field (almost 40%), compared to building, ground, rice field and other habitats. However, these scores may simply reflect the relative importance of the different habitats in the area. No strong conclusion about habitat selection by foxes can thus be drawn from this study. Nevertheless, forest and open-fields were the optimal habitats of the red-backed vole *M. rufocanus*, which is the main intermediate host in Hokkaido.

Stieger et al. (2002) investigated the environmental contamination with faeces of *E. multilocularis* infected foxes and the prevalence in different rodent species in the city of Zurich. The highest prevalence was found for the vole *A. scherman* along the urban periphery. Interestingly, 47 of 604 fox faeces have been found directly on vole ground systems where signs of predation activities of carnivores were observed. This provides evidence that the marking behaviour of foxes could play an important role in the transmission ecology.

Robardet et al. (2011) characterised the impact of environmental factors such as season, habitat, level of urbanisation and abundance of the voles *A. scherman* and *M. arvalis* on the distribution of fox faeces and of copro-ELISA OD values in the urban agglomeration of Nancy (263 000 inhabitants), in the endemic area of northeastern France. They observed a decreasing gradient from east to west in the copro-ELISA OD values. Faeces abundance was higher in winter than in autumn, and copro-ELISA OD values were higher in winter and spring than in autumn, but no impact of the urbanisation level was detected on both parameters. However, faeces abundance was positively correlated with the densities of both *A. scherman* and *M. arvalis*. Several models competed to explain the variations of copro-ELISA OD values, but the most parsimonious model retained the density of *A. scherman*, although the negative correlation observed was unexplained by the authors.

Janko et al. (2011) analysed the space use of 17 foxes in small towns (less than 8600 inhabitants) and their surroundings in southern Germany. In total, 86% of all telemetry bearings were located within the small towns and at a maximum distance of 500 m from the settlement boundary, and the habitats most often used were settlement (35.8%) and forest (31%). No significant difference in the *E. multilocularis* prevalence was observed between foxes in the small village and in the surrounding open countryside (43.1% *vs.* 39.4%).

5. Synthesis and perspectives

This review highlights a number of key issues regarding the transmission ecology of *E. multilocularis* in wild and domestic situations, as well as knowledge gaps that still remain in many fields.

The existence of at least two density-dependent mechanisms acting on the control of the parasite transmission dynamics is described: one is based on the variations in the availability of resources including intermediate hosts (Rausch, 1995; Saitoh and Takahashi, 1998; Miterpakova et al., 2006; Tanner et al., 2006; Hegglin et al., 2007; Guislain et al., 2008; Robardet et al., 2008; Raoul et al., 2010; Stien et al., 2010; Wang et al., 2010; Liccioli et al., 2014), and the other is based on the variations in the density of the definitive host and in their faeces distribution (Ewald, 1993; Raoul et al., 2003; Guislain et al., 2007; Wang et al., 2010). However, we are clearly missing data to predict under which conditions the control of *E. multilocularis* transmission switches from being dominated by intermediate host density to being dominated by definitive host density, and *vice-versa*, in space and/or in time. Additionally, the importance of considering non-linearity and both the direct and delayed response of definitive hosts contamination in relation to intermediate host population variations was noted in eastern France and Japan, respectively (Saitoh and Takahashi, 1998; Raoul et al., 2010).

The dietary response of the red fox was shown to be complex when abundant alternative resources are available, such as in urban settings with anthropogenic food (Hegglin et al., 2007; Robardet et al., 2008) or in a context of choice between several intermediate host prey species, especially when some can undergo population cycles, such as is the case of the grassland areas of eastern France (Raoul et al., 2010). This last point raises the question of the relative contribution of the different small mammal intermediate host species to the parasitic cycle in a context where several species are accessible to predation with densities varying in time, synchronously or not (in short, which species is (are) important in transmission?). In this case, a detailed investigation of the dietary response of the definitive host along with prey population monitoring should provide answers. The difference in the pattern between the dietary response and the parasitic response in definitive hosts, as exemplified in the Jura Mountains with foxes, was also shown (Raoul et al., 2010). Thus, one can scarcely predict the transmission intensity of a trophically transmitted parasite on the single basis of predation patterns. Other factors, such as parasite prevalence, competence and fertility in intermediate hosts and immune response of the definitive host, might be involved, although little information is available.

The investigation of the definitive hosts' activity patterns and defecation behaviour in different landscapes suggested spatial overlap between favoured red fox defecation locations and intermediate host distribution, leading to possible micro-local hotspots

of parasite transmission to intermediate hosts in a landscape (Delattre et al., 1988; LePesteur et al., 1992; Giraudoux et al., 2002; Guislain et al., 2007; Robardet et al., 2011). Additionally, a high spatial and temporal variability in dog faeces density was recorded in Asian study sites where pastoralism is the main activity (China, Kyrgyzstan), with a strong infection pressure in the vicinity of households (Vaniscotte et al., 2011; Van Kesteren et al., 2013). In urban and peri-urban settings, contrasting patterns of the impact of urbanisation level and habitat type on fox distribution or fox faeces density were recorded (Lagapa et al., 2009; Janko et al., 2011; Robardet et al., 2011), but few data are available to draw strong conclusions.

This review also revealed the scarcity of ecological data for dogs. This paucity of data also holds true for coyotes and other definitive hosts. Indeed, over the entire distribution range of *E. multilocularis*, the adult stage of the parasite can be harboured locally by several species of wild and domestic definitive hosts that utilise the same range of habitats. This holds true for red foxes, dogs, raccoon dogs (and cats) in urban and rural settings in Europe, red foxes and coyotes in North America (Liccioli et al., 2012), and dogs, red foxes, Tibetan foxes (*V. ferrilata*) and Corsac foxes (*V. corsac*) in central and western China (Giraudoux et al., 2013). All these definitive hosts exploit the local pool of intermediate host populations, and therefore their local relevance for the transmission of human alveolar echinococcosis must be considered. The impact on *E. multilocularis* transmission dynamics of the functioning of these trophic networks and of the interactions among species remains largely unexplored thus far. For example, the following questions should be addressed: to what extents are domestic and peri-domestic cycles connected to, and maintained by, sylvatic cycles? Does the competition between definitive hosts (*e.g.* coyotes and foxes) for food and habitat resources impact their functional and numerical responses and thus their infection dynamics? How would control measures based on the limitation of one host population density affect the other species involved in the cycle (*via* competition and/or predation release) and thus alter the chances of transmission reduction?

Complementary to the acquisition of more empirical evidence through field data from the entire range of species involved in the parasitic cycle in various transmission systems (Europe, Asia, North America), theoretical work, such as mathematical or agent-based modelling, could help in testing various hypotheses in the topics listed above.

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